

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In Application of:

**Clark T. Hung, et al.** : Group Art Unit: 1744

Serial No.: 10/049,761 : Examiner: W.H. Beisner

Filed: February 7, 2002 : Confirmation No.: 7596

For: **BIOREACTOR FOR GENERATING FUNCTIONAL  
CARTILAGINOUS TISSUE**

**DECLARATION OF CLARK T. HUNG**

Clark T. Hung hereby declares and says:

1. I am an Associate Professor in the Department of Biomechanical Engineering at Columbia University. I have held a faculty position in biomedical engineering since 1997.
2. I received an Sc.B. in Bioengineering from Brown University in 1990. I received an M.S.E. and a Ph.D. in Bioengineering from the University of Pennsylvania in 1992 and 1995, respectively. My doctoral dissertation was entitled "Real-Time Calcium Response to Fluid Flow in Cultured Bone Cells."
3. I have extensive experience in the art of biomedical engineering, especially with regard to the design and preparation of implants to replace or augment cartilaginous tissue in the human body. A copy of my curriculum vitae is attached hereto.

4. I am a co-inventor of the above-identified application.

5. I am familiar with the Office Action dated September 9, 2005, as well as the references cited therein, particularly Lee et al. (PCT published application No. WO 98/401111) (hereinafter referred to as "Lee") and Lee et al. (Journal of Orthopaedic Research) (hereinafter referred to as "Lee and Bader").

6. As explained further herein, the final tissue produced by Lee and Lee and Bader after 48 hours of applied loading is not functional cartilaginous tissue, i.e., tissue as defined in paragraph 29 of my published application as "possessing the mechanical, electrical, chemical, and biochemical properties of cartilaginous tissues -- the properties that permit cartilage to perform and maintain its load-bearing capacity."

7. Based on my experience, one of ordinary skill in the art of biomedical engineering considers the properties described in paragraphs 8, 9, and 10 to determine whether cartilaginous tissue produced in a bioreactor is functional cartilaginous tissue.

8. The mechanical properties of cartilaginous tissue include a compressive Young's modulus, which is a measure of stiffness. For native tissue, the compressive Young's modulus ranges from about 200 to about 1400 kPa, as described in paragraph 5 of my published application. These properties also include a hydraulic permeability, which is a measure of resistance to fluid flow through the tissue. For native tissue, the hydraulic permeability ranges from about  $10^{-15}$  to about  $10^{-16} \text{ m}^4/\text{Ns}$ , as described in paragraph 6 of my published application.

9. The electrical properties of cartilaginous tissue include a streaming potential, which is the measured voltage generated by the flow of a charged ionic solution (e.g., a bathing solution in culture or a native interstitial fluid) through the GAG-rich (i.e., glycosaminoglycan-rich) matrix of cartilage during applied deformational loading.

10. The chemical and biochemical properties of cartilaginous tissue include a GAG content, which is a measure of proteoglycan content. For native tissue, the GAG content ranges from about 2.5 to about 10 % tissue wet weight (ww). These properties also include a collagen content. For native tissue, the collagen content ranges from about 5 to about 30 % ww.

11. Based on my experience, one of ordinary skill in the art of biomedical engineering customarily determines whether cartilaginous tissue produced in a bioreactor is functional cartilaginous tissue by quantitatively comparing the properties exhibited by that tissue with the properties exhibited by native tissue.

12. For example, based on my experience, one of ordinary skill in the art customarily considers tissue having a GAG content approaching about 1 % ww to be functional cartilaginous tissue. This threshold of functional GAG content is about an order of magnitude smaller than the upper range of the GAG content of native tissue.

13. A customary method for measuring the sulfated GAG content of cartilaginous tissue is to perform a so-called colorimetric assay. In such an assay, a sample of cartilaginous tissue is wet weighed, digested with an enzyme, exposed to a

standard colored dye (e.g., dimethylmethylen blue), and then observed with a spectrophotometer. GAG molecules in the sample bind to the dye and cause a color change in the sample that can be measured with the spectrophotometer. The GAG content of the sample can be determined from a calibration curve of spectrometer measurement readings and known standard concentrations of GAG.

14. Lee produces a tissue product after 48 hours of applied loading. (See, e.g., Lee examples 6 and 10.) Lee does not provide any quantifiable evidence from which one of skill in the art could conclude the final tissue product to be functional based on its mechanical, electrical, chemical, and/or biochemical properties.

15. More specifically, Lee does not provide any quantifiable evidence at all related to the mechanical, electrical, chemical, and biochemical properties of the final tissue product after 48 hours of applied loading. At most, Lee provides graphs of cell metabolic activity in Figs. 8a and 8b that merely show increased sulfate incorporation (a measure of GAG synthesis rate) and thymidine incorporation (a measure of DNA synthesis rate), respectively, in dynamically loaded constructs compared to the unloaded (control) scaffold. Since these radiolabel incorporation assays represent only the metabolic state of the cells, the graphs do not provide any basis for a quantitative determination of the GAG content (i.e., actual GAG that has been deposited by the cells into the construct) of the final tissue product after 48 hours of applied loading.

16. Based on my experience and the foregoing observations, one of ordinary skill in the art would not consider the final tissue product of Lee to be functional cartilaginous tissue.

17. Lee and Bader also produce a tissue product after 48 hours of applied loading. (See, e.g., Lee and Bader "Results.") Like Lee, Lee and Bader do not provide any quantifiable evidence from which one of skill in the art could conclude the final tissue product to be functional based on its mechanical, electrical, chemical, and/or biochemical properties.

18. More specifically, Lee and Bader do not provide any quantifiable evidence related to the mechanical and electrical properties of the final tissue product after 48 hours of applied loading.

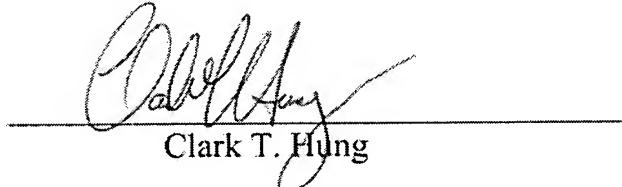
19. Lee and Bader do, however, provide quantifiable evidence of chemical and biochemical properties of the final tissue product after 48 hours of applied loading. As described in the Lee and Bader "Results" section, the final tissue product has a GAG content of  $42.8 \times 10^{-6}$  g GAG/ $10^6$  cells. Lee and Bader specify the relationship between cell density and construct wet weight to be  $1 \times 10^6$  cells = 0.255 g. (See Lee and Bader, p. 183, col. 2, ll. 2-5). Using this conversion factor, the Lee and Bader final tissue product has a GAG content of  $(42.8 \times 10^{-6}$  g GAG/ $10^6$  cells)  $\times$   $(1 \times 10^6$  cells/0.255 g) = 0.017 % ww. Lee and Bader do not provide any quantifiable evidence of other chemical and/or biochemical properties of the final tissue product.

20. As noted in paragraph 12, the threshold GAG content of functional cartilaginous tissue is about 1 % ww. The GAG content of the Lee and Bader final tissue product (i.e., 0.017 % ww) is, therefore, about two orders of magnitude smaller than the threshold GAG content of functional cartilaginous tissue.

21. Based on my experience and the foregoing observations, one of ordinary skill in the art would not consider the final tissue product of Lee and Bader to be functional cartilaginous tissue.

22. In summary, neither Lee nor Lee and Bader teaches or suggests the production of functional cartilaginous tissue.

Date: March 9, 2006



---

Clark T. Hung

# CLARK T. HUNG, PH.D.

2/14/06

Department of Biomedical Engineering  
351J Engineering Terrace MC8904  
1210 Amsterdam Avenue  
New York, NY 10027  
(212) 854-6542; fax (212) 854-8725  
<http://cellsrv.bme.columbia.edu>; [cth6@columbia.edu](mailto:cth6@columbia.edu)

35 Sheffield Court  
Ardsley, NY 10502  
(914) 980-5550

## FIELD OF SPECIALIZATION

Physical effects on cells and orthopaedic cell mechanotransduction and tissue engineering.

## ACADEMIC TRAINING

University of Pennsylvania *Philadelphia, PA*  
PH.D., BIOENGINEERING, 12/95.  
Dissertation: *Real-Time Calcium Response to Fluid Flow in Cultured Bone Cells.*  
Advisor: Drs. Solomon R. Pollack and Carl T. Brighton

University of Pennsylvania *Philadelphia, PA*  
M.S.E., BIOENGINEERING, 5/92.  
Advisor: Dr. John L. Williams

Brown University *Providence, RI*  
SC.B., BIOENGINEERING, 5/90.

## HONORS/AWARDS

- 1990-95 NIH Bone & Cartilage Traineeship (Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA)
- 1996 Postdoctoral Fellowship (NASA- Wistar Institute-Bioengineering, University of Pennsylvania, Philadelphia, PA)
- 1996 Solomon R. Pollack Award for Excellence in Graduate Bioengineering Research (Department of Bioengineering, University of Pennsylvania, Philadelphia, PA)
- 1997 Whitaker Special Opportunity Award Postdoctoral Fellowship (Center for Biomedical Engineering, Columbia University, New York, NY)
- 2000 Guest editor with Drs. Farshid Guilak and Ray Vanderby for special Cell & Tissue Engineering issue of *J Biomech Eng* (June 2000).
- 2002 Edward and Carole Kim Award for Faculty Involvement (Fu Foundation School of Engineering & Applied Science, Columbia University, New York, NY)
- 2003 NEGMA-LERADS Prize; 3<sup>rd</sup> International Symposium on Mechanobiology of Cartilage and Chondrocyte, Brussels, Belgium, May 16-17, 2003.
- 2004 Co-author, The John Paul Stapp Best Paper Award in the 2003 Stapp Car Crash Journal presented at the 47th Stapp Car Crash Conference. *A tissue level tolerance criterion for living brain developed with an in vitro model of traumatic mechanical loading* (Morrison III, B lead author)
- 2005 Invited White Paper Author and Moderator: Biomechanics Curriculum Workshop at the Whitaker Foundation Educational Summit II, Lansdowne, VA, March 3-6, 2005.

## PROFESSIONAL SOCIETIES/ACTIVITIES

American Society for Mechanical Engineers (ASME): Bioengineering Division- Cell and Tissue Engineering Committee, Biomedical Engineering Society (BMES), Orthopaedic Research Society (ORS)

Ad-hoc Reviewer: *Clin Orthop Rel Res, Biophys J, J Biomechanics, J Orthop Res, J Biomech Eng, Arthritis Research, Arthritis Rheumatism, Biochem Biophysica Acta, J Microscopy, Bone, J Bone Miner Res, Osteoarthritis Cartilage, Calcified Tissue, Ann Biomed Eng, Tissue Eng, Acta Biomaterialia, Med Eng Physics*

1999 Session Organizer and Chair, ASME Summer Bioengineering Conference 1999 (Redmond, MT): 6 *Tissue Engineering* sessions with Drs. Farshid Guilak and Ray Vanderby

1999 Session Organizer and Chair, 1999 ASME Winter Meeting (Nashville, TN) 2 sessions on *Cell Mechanics*

2000 Session Organizer and Chair, 2000 ASME Winter Meeting (Orlando, FL): a) *Cell Mechanics*; b) *Tissue Engineering*

2001 Session Moderator, *Cartilage Mechanics*, 47<sup>th</sup> Annual Meeting of the Orthopaedic Research Society (San Francisco, CA).

2001 Session Organizer and Chair, 2001 ASME Summer Bioengineering Conference (Snowbird, Utah): a) *Orthopaedic Tissue Engineering*; b) *Cellular Engineering*

2001 Session Organizer and Chair for 2001 BMES Annual Meeting (Durham, NC): *Mechanotransduction III*

2001 Session Chair, 2001 ASME Winter Meeting (New York, NY): *Tissue Engineering*

2001 Ad hoc Reviewer for Singapore Biomedical Research Council Grants (September)

2002 Session Moderator: *Cartilage Mechanics*, 48<sup>th</sup> Annual Meeting of the Orthopaedic Research Society (Dallas, TX).

2002 Session Organizer, 2002 ASME Winter Meeting (New Orleans, LA): a) *Cellular Engineering & Mechanics*; b) *Tissue Engineering*

2003 Session Organizer and Chair, 2003 ASME Summer Bioengineering Conference (Key Biscayne, FL): *Orthopaedic Cell & Tissue Engineering*- 2 sessions.

2003 Phone Reviewer for National Institute of Dental and Craniofacial Research (NIDCR) R03 grant applications, July 19.

2003 Reviewer for CSR special emphasis panel ZRG1 SSS-U(40) for biomedical technology resource grant (NIH P41) at Tufts University (July 21-23).

2003 Reviewer for abstract submissions to 50<sup>th</sup> Annual meeting of the Orthopaedic Research Society

2004 Phone Reviewer for National Institute of Dental and Craniofacial Research (NIDCR) R03 grant applications, February 19.

2004 Reviewer for CSR special emphasis panel ZRG1 BST-D (40) for biomedical technology resource grant (NIH P41) (Old Town, VA, April 7-8).

2004 Mail Reviewer: for South Carolina NASA/EPSCoR Research Grant Program

2004 Mail Reviewer: for CSR Skeletal Biology Development and Disease (SBDD) study section R21 grant applications, June 27.

2004 Co-Chair/Organizer: 3 sessions on Orthopaedic Mechanobiology at 2004 BMES Annual Meeting (Philadelphia, PA)

2004 Reviewer for abstract submissions to 51<sup>st</sup> Annual meeting of the Orthopaedic Research Society

2004 Mail Reviewer: Aircast Foundation

2004 Mail Reviewer: Swiss National Science Foundation, Division of Biology and Medicine

2005 Session Moderator: *Molecular and Cellular Mechanics*, 51<sup>st</sup> Annual meeting of the Orthopaedic Research Society (Washington, D.C.)

2005 Phone Reviewer: NIBIB (Marc Rigas, NIH/CSR); March 28, 2005.

2005 Session Chair: 2005 Summer Bioengineering Conference, Vail, CO: *Cell and Molecular Engineering I & II, Cartilage Tissue Engineering*

2005      Phone Reviewer: Reviewer for CSR Telephone special emphasis panel (ZRG1 MOSS-K 04), July 15

2005      Reviewer for abstract submissions to 52<sup>nd</sup> Annual meeting of the Orthopaedic Research Society

2005-     Vice Chairman, Cell and Tissue Engineering Committee, Bioengineering Division of the American Society for Mechanical Engineers

2006-     Associate Editor, *Journal of Biomechanical Engineering* (term to begin Januray 1)

## PATENTS

A full US patent application entitled: *Bioreactor for Generating Functional Cartilaginous Tissue* by Hung et al. has been submitted February 7, 2002.

## INVITED LECTURES

1. Seminar Speaker: *Real-Time Calcium Response to Fluid Flow in Cultured Bone Cells*; The Hospital for Special Surgery, New York, NY, August 12, 1995
2. Seminar Speaker: *Real-Time Calcium Response to Fluid Flow in Cultured Bone Cells*; Columbia University, Department of Mechanical Engineering, New York, NY, December 2, 1995
3. Seminar Speaker: *Real-Time Calcium Response to Fluid Flow in Cultured Bone Cells*; Tulane University, Department of Biomedical Engineering, New Orleans, LA, September 10, 1996
4. Seminar Speaker: *Anterior Cruciate and Medial Collateral Ligament Fibroblasts Exhibit Different Calcium Responses to Fluid Flow*; Columbia University, Center for Biomedical Engineering, New York, NY, January 23, 1997
5. Seminar Speaker: *Chondrocyte Response to Fluid-induced Shear Stress*, Advanced Tissue Sciences, LaJolla, CA, June 1997
6. Seminar Speaker: *Real-Time Calcium Response to Fluid Flow in Cultured Bone Cells*; Indiana Bone & Mineral Group, Indianapolis, IN, February 24,1999
7. Guest lecturer in BME 1001 Engineering in Medicine, *Cartilage Tissue Engineering*; Department of Biomedical Engineering, New York, NY, February 28, 2000.
8. Seminar Speaker: *Chondrocyte Response to Osmotic Loading: Experimental and Theoretical Studies*; University of Massachusetts Medical Center, Worcester, MA, January 29, 2001
9. Invited Speaker: *Functional Tissue Engineering of Articular Cartilage*; University of Nancy, France, April 23, 2001.
10. Plenary Speaker: *Functional Tissue Engineering of Articular Cartilage*; EuroMech Colloquium 420: Mechanobiology of Cells and Tissues, Nancy, France, April 25,2001
11. Invited Speaker: *Determination of the Chondrocyte Environment within Cartilage Subjected to Loading: Theoretical and Experimental Approach*; 2<sup>nd</sup> International Symposium on Mechanobiology of Chondrocytes and Cartilage, Paris, France, April 27, 2001.
12. Invited Speaker: *Cell & Tissue Culture Techniques: A Tutorial*; 2001 ASME Summer Bioengineering Conference, Snowbird, UT, June 29, 2001.
13. Invited Speaker: *Functional Tissue Engineering of Articular Cartilage*; Columbia Class of 1951 Reunion, Arden House, Harriman, NY, September 8, 2001.
14. Invited Speaker: *Fluid Flow Effects on Bone Cells: Influence of Flow-Cell-Substrate Interactions and Cell Mechanical Properties*; Fluid Flow in Bone Workshop, Phoenix, AZ, October 11, 2001.
15. Invited Speaker: *Fluid Flow Effects on Bone Cells: Influence of Flow-Cell-Substrate Interactions and Cell Mechanical Properties*; NYC Mineralized Tissue Seminar, New York, NY, December 12, 2001.
16. Invited Speaker: *Tutorial: Biomechanical Factors in Tissue Engineering: Bioreactors*; 48<sup>th</sup> Annual Meeting of the Orthopaedic Research Society Meeting, Dallas, TX, February 10, 2002.

17. Invited Speaker: *A Paradigm for Functional Tissue Engineering of Articular Cartilage*, Stanford University Bio X Sponsored Symposium on Cartilage Tissue Engineering, Palo Alto, CA, March 22, 2002.
18. Invited Speaker: *Biomechanical Factors in Tissue Engineering: Bioreactors*; Biomedical Technology Track sponsored Bioreactor Design Tutorial at the 2002 Winter Annual ASME Meeting, New Orleans, LA, November 20, 2002.
19. Invited Speaker: *A Paradigm for Functional Tissue Engineering of Articular Cartilage*, Department of Mechanical Engineering, Georgia Institute of Technology, Atlanta, GA, April 22, 2003.
20. Invited Speaker: NEGMA-LERADS prize lecture: *A Paradigm for Functional Tissue Engineering of Articular Cartilage*, 3<sup>rd</sup> International Symposium on Mechanobiology of Cartilage and Chondrocyte, Brussels, Belgium, May 16-17, 2003.
21. Invited Speaker: *A Paradigm for Functional Tissue Engineering of Articular Cartilage using Applied Deformational Loading*, 4th International Conference on Tissue and Genetic Engineering, Boston, MA, April 1-2, 2004.
22. Invited Lecture: *Engineering Biological Replacements for Joints*, Columbia University Southern California Dean's Day Symposium, West Hollywood, CA, March 13, 2004.
23. Invited Lecture: *A Functional Tissue Engineering Strategy for Repair and Replacement of Osteoarthritic Cartilage*, European Society of Biomechanics 2004, the Netherlands, July 4-7, 2004.
24. Invited Lecture: *Chondrocyte Mechanotransduction: Cartilage Basic Science to Tissue Engineering*, Department of Biomedical Engineering, Purdue University, West Lafayette, IN, September 24, 2004.
25. Invited Lecture: *Chondrocyte Mechanotransduction: Cartilage Basic Science to Tissue Engineering*, Brown University, May 5-6, 2005.
26. Invited Speaker: *Chondrocyte Mechanotransduction: Cartilage Basic Science to Tissue Engineering*, Society of In Vitro Biology Conference, June 4-7, 2005, Baltimore, MD
27. Invited Speaker: *Cartilage Biomechanics and Tissue Engineering*, Stryker Medical, Mahwah, NJ, July 22, 2005.
28. Invited Speaker: *Cartilage Tissue Engineering: Implications of Applied Deformational Loading and Solute Transport*. McGowan Institute for Regenerative Medicine, University of Pittsburgh, October 6, 2005.
29. Invited Speaker: *Cartilage Tissue Engineering: Implications of Applied Deformational Loading and Solute Transport*. Department of Orthopaedic Surgery Grand Rounds and Department of Biomedical Engineering Seminar Series, University of California-Irvine, December 1, 2005.

## TEACHING RECORD

1. BMEN 4001,3001 Biomedical Engineering Principles I – (Fall ‘99,’00) quantitative molecular/cell biology- enrollment 40 students
2. BMEN 4002,3002 Biomedical Engineering Principles II – (Spring ‘98,’99) quantitative physiology- enrollment 40 students
3. BMEN 4501 Tissue Engineering I (Fall ‘98, ‘99,’00, ‘01, ‘02,’03, ‘04)- current enrollment 74 students and taught as an offering of the Columbia Video Network (CVN).
4. BMEN 3820 Biomedical Engineering Laboratory II (Spring ‘01,’02,’03,’04)- current enrollment 58 students
5. BMEN 3830 Biomedical Engineering Laboratory III (Fall ‘99)- enrollment 40 students
6. BMEN 4502 Tissue Engineering II (Spring ‘00) - enrollment 50 students
7. BMEN 3840 Biomedical Engineering Laboratory (Spring ‘99)- enrollment 40 students
8. BMEN 3998 Independent Research Advisor: (Spring ‘00- present) – 3 students/semester

9. BMEN 3910 Senior Design (Spring '99- present): 5 students- Advisor for projects aimed at chamber for osmolarity studies ('98), a methodology to make alginate slabs ('99); device to measure direct hydraulic permeability of soft hydrated tissues ('00), alginate hollow microspheres ('01,'02,'03). For Spring '04: *in vitro* cartilage repair (4 students) model, pressure/deformation bioreactor design (4 students) and sperm motility projects (4 students)
10. G3200 Cellular Sensing, Transduction, and Amplification of Mechanical Forces (Spring '05; City College of New York biomedical engineering course directed by Professor Sheldon Weinbaum): instructor for module on cartilage mechanotransduction (10 students).
11. Summer BME High School Course: *Physical Effects on Cells* (July 99- present)- 20-24 high school students per year. Course developed and administered through the Columbia High School Programs, Columbia Continuing Education and Special Programs. The month long course provides an introduction to the multidisciplinary field of biomedical engineering and the application of engineering principles to solving problems in biology, physiology, and medicine. International students have also participated in this course. Teaching assistants are BME undergraduate or graduate students.

## FELLOWS/STUDENTS/ STAFF SUPERVISED

### Postdoctoral Fellows: present position

1. Glyn D. Palmer, Ph.D. (9/99-12/00): Postdoctoral fellow at Center for Molecular Orthopaedics, Harvard Medical School, Boston, MA
2. Michelle A. LeRoux-Williams, Ph.D. (9/00-10/01): Development engineer at Osiris Therapeutics, Baltimore, MD
3. Christopher C-B. Wang, Ph.D. (8/01-6/03 ): Research analyst, American Express, New York, NY

### Doctoral Students: dissertation title

1. Co-Advisor: Christopher C-B. Wang (7/99- 8/01): Ph.D. thesis in Mechanical Engineering: *Functional properties of cartilage and environment of chondrocytes: experiments and theoretical analyses*
2. Co-Advisor: Robert L. Mauck (8/98-7/29/03): Ph.D. thesis in Biomedical Engineering: *Functional tissue engineering of articular cartilage: The effect of physical forces on the in vitro growth of engineered constructs*
3. Advisor: Pen-Hsiu Grace Chao (1/99-8/05 ): Ph.D. thesis in Biomedical Engineering: *Physical forces on cells: effects of applied osmotic loading and direct current electric fields*
4. Advisor: Terri-Ann N. Kelly (1/00- )- BME doctoral candidate
5. Co-Advisor: Nadeen O. Chahine (9/00- ): BME doctoral candidate
6. Co-Advisor: Eric G. Lima (9/01-): BME doctoral candidate
7. Advisor: Kenneth W. Ng (9/01-): BME doctoral candidate
8. Advisor: Mandy Ho (9/02-): BME doctoral candidate
9. Advisor: Elizabeth S. Oswald (9/04-): BME doctoral candidate
10. Advisor: Liming Bian (1/05-): BME doctoral candidate

### Master's Students: present position

1. Louis Cappezuto, J.D. (1/02-5/02): M.S., Biotechnology Program (consul at Johnson and Johnson)
2. Amir Hakakha, M.S.E. (1/01-9/01): Ortec, Manager of Technology Development, New York, NY
3. HyukJin Lee, M.S.E. (8/03-5/04): Recently Graduated
4. Shelley Han, M.S.E., (1/02-7/04): Industry
5. Patricia B. Setti, M.S.E., (9/04-12/04): Stryker Orthopaedics (Regulatory Affairs), Mahwah, NJ

### Undergraduate Students: present position

1. Rani Roy, FFSEAS '00: Ph.D. candidate at Cornell University BME

2. Sarah Desoky, FFSEAS '00: NA
3. Lia Hondroulis, FFSEAS '00: Andrx Pharmaceuticals (candidate for law school)
4. Wendy Liu (MIT '00, summer 1999): Ph.D. candidate at Johns Hopkins BME
5. Dennis Wong, FF SEAS '01: Working at the National Security Agency
6. Brian Kim, FF SEAS '01: Premed coursework at Columbia
7. Aparna Prasad, FF SEAS '01: Medical student at SUNY Buffalo Medical School
8. Nelly Andarawis, FF SEAS '01: Ph.D. candidate at University of Pennsylvania BME
9. Kelly Jamieson, FF SEAS '02: Research Technician at Mt. Sinai Medical Center
10. Laura Rummel, FF SEAS '02: Research engineer at Peripheral Nerve Research Laboratory, UC Irvine; Doctoral candidate UC Irvine
11. Nicole Gabriel (Rice University '03, summer 2002): Ph.D. candidate at University of Pennsylvania BME
12. Elizabeth Oswald, FF SEAS '04: Will be attending Columbia University BME as a doctoral candidate in the fall.
13. QiQi Cheng, FF SEAS '04: Ph.D. candidate at University of Pennsylvania BME
14. Christopher DuBois, FF SEAS '04: Ph.D. candidate at University of Pennsylvania BME
15. Selom Gasinu, FF SEAS '04: Attending Temple Medical School
16. Michael Bazylewicz, FF SEAS '04 (summer 2004): Attending Dartmouth College Medical School
17. Mathew Fisher, FFSEAS'05: Will be attending University of Pittsburgh BME as a doctoral candidate
18. Lauren Statman, FFSEAS '05: Will be attending UCSF Bioengineering as a doctoral candidate
19. Anne-Marie Cannon (Rice University '05, summer 2003): employed at Xenogen Biosciences, in Cranbury NJ
20. Fran Navratil, FFSEAS '04: MTV, New York, NY
21. Jesse Martin, FFSEAS'05
22. Timon Tai, FFSEAS '06
23. Gilad Landan FFSEAS '06
24. Whitney Booker, FFSEAS '05

Medical Students: present position

1. Frank Raia, M.D.: Orthopaedic resident at Columbia-Presbyterian
2. Ross Henshaw, M.D.: Orthopaedic resident at Columbia-Presbyterian
3. Sansan S. Lo, M.D.: (9/00-5/01): Orthopaedic resident at Columbia-Presbyterian

Orthopaedic Residents

1. Justin Saliman, M.D.: (1/04-3/04) Orthopaedic resident at St. Luke's-Roosevelt
2. David Capiola, M.D.: (3/04-5/04) Orthopaedic resident at St. Luke's-Roosevelt
3. Steve Quinnan, M.D.: (1/05-3/05) Orthopaedic resident at St. Luke's-Roosevelt
4. Darren Friedman, M.D.: (3/05-5/05) Orthopaedic resident at St. Luke's-Roosevelt

Lab Manager: present position

1. Sara Seyhan, B.S.E.: (2/00-2/02) Associate Engineer at Anterogen Co., Ltd.

## DISSERTATION COMMITTEES

1. Michael Huang (MSE, '98): *Development of an apparatus and technique to measure calcium binding in skeletal and cardiac muscle* (examiner)
2. Andrey Levchenko (DES, '98): *Expression and action of P-glycoprotein: A quantitative analysis*
3. Hong An (Ph.D., '99; Chem Eng): *Cell deformation in an asymmetric thin liquid film* (examiner)
4. Shawn Gomez (EngScD , '99): *Attachment of cells to surfaces under controlled fluid flows* (examiner)

5. Sarah Patrick (Ph.D., '99): *Control of receptor-ligand contact to examine the kinetics of T cell activation* (examiner)
6. Michael Soltz (Ph.D., '00; Mech Eng): *Investigation of a boundary friction model for articular cartilage: Effects of interstitial fluid pressurization and surface topography* (examiner)
7. Chun-Yuh Huang (Ph.D., '01): *Biomechanics of soft tissues in the shoulder joint-glenohumeral cartilage, ligament, and rotator cuff tendon* (examiner)
8. Sabin Kim (Ph.D., '01; Chem Eng): *Kinetics of calcium mobilization of a T cell activated by controlled receptor-ligand contact* (examiner)
9. Vincent Wang (Ph.D., '01; Mech Eng): *Biomechanics of the normal and surgically reconstructed shoulder* (examiner)
10. Stavroula Sofou (Ph.D., '01; Chem Eng): *Control of phospholipid vesicle organization with cysteine-containing oligopeptides* (examiner)
11. Changbin Wang (Ph.D., '01; Mech Eng): *Digital video microscopy-based determination of cartilage inhomogeneity, anisotropy and tension-compression nonlinearity: Implications on chondrocyte environment* (co-sponsor)
12. Chi Hyun Kim (EngScD, '03; Mech Eng): *In vivo trabecular bone response to mechanical loading and parathyroid hormone stimulation* (chairman, examiner)
13. Zhongliang Tang (Ph.D., '03; Chem Eng): *Microfluidics: fluid flow, transport, control, characterization and applications* (examiner)
14. Robert Mauck (Ph.D., '03): *Functional tissue engineering of articular cartilage: The effect of physical forces on the in vitro growth of engineered constructs* (co-sponsor)
15. Vedran Knezevic: Doctoral proposal: *A system for biaxial loading of fibroblast-populated collagen gels for the study of mechanobiology* (examiner)
16. Pen-Hsiu Grace Chao (Ph.D., '05): Doctoral proposal: *Physical forces on cells: effects of applied osmotic loading and direct current electric fields* (sponsor)
17. Mia Mia Thi (City College of New York): Doctoral proposal: *Effects of fluid shear stress on bone cell gap junctional communication* (examiner)
18. Patrick Johnson (Ph.D., '04; Chem Eng): *Polymer-anchored DNA monolayers for electrochemical sensing* (examiner)
19. Peng Wang (Ph.D., '04; Chem Eng): *Polymeric thin films: preparations, surface modification and morphology* (examiner)
20. Erica Takai (Ph.D., '05): *Modulation of Bone Cell Mechanotransduction* (examiner)
21. Seonghun Park (Ph.D., '05, Mech Eng)): Doctoral pre-proposal and proposal: *Interstitial fluid flow-dependent and flow-independent mechanical and tribological response of articular cartilage* (Mech Eng) (examiner)
22. Nadeen Chahine: *Cartilage Biomechanics* (Biomed Eng) (co-sponsor)
23. Terri-Ann Kelly: Doctoral pre-proposal (Biomed Eng): *Characterization and optimization of chondrocyte-seeded agarose constructs grown in free-swelling and dynamic-loading culture* (sponsor)

## EMPLOYMENT RECORD

1995      Instructor, Department of Bioengineering, University of Pennsylvania, Philadelphia, PA (Fall)

1996      Postdoctoral Fellow, Department of Bioengineering, University of Pennsylvania, Philadelphia, PA (NASA microgravity-bioreactor studies- 1/96-6/96); Postdoctoral Fellow, Orthopaedic Research Laboratory, Center for Biomedical Engineering, Columbia University, New York, NY (cartilage research- 7/96-6/97)

1997-2002 Assistant Professor of Biomedical Engineering, Fu Foundation School of Engineering & Applied Science (FFSEAS); Associate, Orthopaedic Research; Columbia University, New York, NY (appointed 7/97)

1998-      Director, Cellular Engineering Laboratory, FFSEAS

1999- Director, July summer high school course *Physical Effects on Cells: Biomedical Engineering*, Columbia University, New York, NY  
 1999-2003 Department of Biomedical Engineering undergraduate and graduate committee member, sophomore class advisor, Biomedical Engineering Society (BMES) faculty advisor  
 2000- Cellular Engineering Faculty Search Committee Member, Department of Biomedical Engineering, FFSEAS  
 2000- Faculty advisor for Biomedical Engineering graduate students association (GraBME).  
 2002- Associate Professor of Biomedical Engineering, FFSEAS  
 2004- Associate Professor of Biomedical Engineering with tenure, FFSEAS (May)  
 2004- Member, Nominating Committee, FFSEAS  
 2003-2005 Chair, Undergraduate Committee, Department of Biomedical Engineering, FFSEAS

## JOURNAL ARTICLES

1. Hung CT, Williams JL: A method for inducing equi-biaxial and uniform strains in elastomeric membranes used as cell substrates. *J Biomechanics* 27(2):227-232, 1994.
2. Hung CT, Pollack SR, Reilly TM, Brighton CT: Real-time calcium response of cultured bone cells to fluid flow. *Clin Orthop Rel Res* 313:256-269, 1995.
3. Hung CT, Allen FD, Pollack SR, Brighton CT: What is the role of the convection current density in the real-time calcium response of cultured bone cells to fluid flow? *J Biomechanics* 29(11):1403-1409, 1996.
4. Hung CT, Allen FD, Pollack SR, Brighton CT: Intracellular  $\text{Ca}^{2+}$  stores and extracellular  $\text{Ca}^{2+}$  are required in the  $[\text{Ca}^{2+}]_i$  response of bone cells experiencing fluid flow. *J Biomechanics* 29(11):1411-1417, 1996.
5. Allen FD, Hung CT, Pollack SR, Brighton CT: Comparison of the  $[\text{Ca}^{2+}]_i$  response to fluid flow of MC3T3-E1, ROS 17/2.8, and cultured primary osteoblast-like cells. *Cell Eng* 1:117-124, 1996.
6. Hung CT, Allen FD, Mansfield K, Shapiro IR: Extracellular ATP modulates  $[\text{Ca}^{2+}]_i$  in retinoic acid treated embryonic chondrocytes. *Am J Physiol* 272 (5 Pt 1): C1611-C1617, 1997.
7. Hung CT, Allen FD, Pollack SR, Attia ET, Hannafin JA, Torzilli PA: Anterior cruciate and medial collateral ligament fibroblasts exhibit different  $\text{Ca}^{2+}$  responses to fluid flow. *Cell Signal* 9(8):587-594, 1997.
8. Mow VC, Wang, CC, Hung CT: The extracellular matrix, interstitial fluid and ions as a mechanical signal transducer in articular cartilage. *Osteoarthritis Cartilage* 7:41-59, 1999.
9. Hung CT, Henshaw DR, Wang CC-B, Mauck R, Raia F, Palmer G, Mow VC, Ratcliffe A, Valhmu WB: Mitogen-activated protein kinase signaling in bovine articular chondrocytes in response to fluid flow does not require calcium mobilization. *J Biomechanics* 33:73-80, 2000.
10. Chao P-HG, Roy R, Mauck RL, Liu W, Valhmu WB, Hung CT: Chondrocyte translocation response to direct current electric fields. *J Biomech. Eng.* 122:261-267, 2000.
11. Mauck RL, Soltz MA, Wang CC-B, Wong DD, Chao P-HG, Valhmu WB, Hung CT, Ateshian GA: Functional tissue engineering of articular cartilage through dynamic loading of chondrocyte-seeded agarose gels. *J Biomech Eng* 122:252-260, 2000.
12. Allen FD, Hung CT, Pollack SR, Brighton CT: Mechano-chemical coupling in the flow-induced activation of intracellular calcium signaling in primary cultured bone cells. *J Biomechanics* 33(12):1585-1591, 2000.
13. Wang CC-B, Hung CT, Mow VC: Inhomogeneity of aggregate modulus affects cartilage compressive stress-relaxation behavior. *J Biomechanics* 34(1): 75-84, 2001.
14. Palmer GD, Chao P-HG, Raia F, Mauck RL, Valhmu WB, Hung CT: Time dependent aggrecan gene expression of articular chondrocytes subjected to hyperosmotic loading. *Osteoarthritis Cartilage* 9(8): 761-770, 2001.

15. Wang CC-B, Guo, XE, Sun, D, Mow VC, Ateshian GA, Hung CT: The functional environment of chondrocytes within cartilage subjected to compressive loading: theoretical and experimental approach. *Biorheology*, 39(1-2):39-45, 2002.
16. Wang CC-B, Ateshian GA, Hung CT: An automated approach for direct measurement of strain distributions within articular cartilage under unconfined compression. *J Biomech Eng* 124:557-567,2002.
17. Mauck RL, Seyhan SL, Ateshian GA, Hung CT: The influence of seeding density and dynamic deformational loading on the developing structure/function relationships of chondrocyte-seeded agarose hydrogels. *Ann Biomed Eng* 30:1046-1056, 2002.
18. Chafik D, Bear D, Bui P, Patel A, Jones NF, Kim BT, Hung CT, Gupta R, Optimization of schwann cell adhesion in response to shear stress in an in vitro model for peripheral nerve tissue engineering. *Tissue Eng* 9(2):233-241, 2003.
19. Ateshian GA, Soltz MA, Mauck RL, Hung CT, Lai WM: The role of osmotic pressure in the frictional response of articular cartilage. *Transport Porous Media* 50:5-33,2003.
20. Hung CT, LeRoux MA, Palmer GD, Chao PG, Valhmu WB: Disparate aggrecan gene expression in chondrocytes subjected to hypotonic and hypertonic loading in 2D and 3D culture. *Biorheology* 40(1-3): 61-72, 2003.
21. Wang CCB, Chahine NO, Hung CT, Ateshian GA: Optical determination of anisotropic material properties of bovine articular cartilage in compression, *J Biomechanics* 36(3): 339-353, 2003.
22. Mauck RL, Nicoll SB, Seyhan SL, Ateshian GA, Hung CT: Synergistic effects of growth factors and dynamic loading for cartilage tissue engineering. *Tissue Eng* 9(4), 597-611, 2003.
23. Mauck RL, Hung CT, Ateshian GA: Modeling of neutral solute transport in a dynamically loaded porous permeable gel. *J Biomech Eng* 125(5): 602-614, 2003.
24. Hung CT, Lima EG, Mauck RL, Takai E, LeRoux MA, Lu HH, Stark RG, Guo XE, Ateshian GA: Anatomically shaped osteochondral constructs for articular cartilage repair. *J Biomechanics* 36(12): 1853-1864, 2003.
25. Mauck RL, Wang CC-B, Oswald ES, Ateshian GA, Hung CT: The role of cell seeding density and nutrient supply for articular cartilage tissue engineering with deformational loading *Osteoarthritis Cartilage* 11(12): 879-890, 2003.
26. Morrison III B, Cater HL, Wang CC-B, Thomas FC, Hung CT, Ateshian GA, Sundstrom LE: A tissue level tolerance criterion for living brain developed with an in vitro model of traumatic mechanical loading. *Stapp Car Crash Journal* 47: 93-105, 2003.
27. Park S, Hung CT, Ateshian GA: Mechanical response of bovine articular cartilage under dynamic unconfined compression loading at physiologic stress levels. *Osteoarthritis Cartilage*, 12(1):65-73, 2004.
28. Ateshian GA, Chahine NO, Basalo IM, Hung CT: The correspondence between equilibrium biphasic and triphasic material properties in mixture models of articular cartilage. *J Biomechanics* 37, 391-400, 2004.
29. Hung CT, Mauck RL, Wang CC-B, Lima EG, Ateshian GA: A paradigm for functional tissue engineering of articular cartilage via applied physiologic deformational loading. *Ann Biomed Eng* 32(1), 35-49, 2004.
30. Finkelstein E, Chang W, Chao PHG, Gruber D, Hung CT, Bulinski C: Roles of microtubules, cell polarity, and adhesion in electric field-mediated motility. *J Cell Science* 117(8),1533-1545, 2004.
31. Chahine NO, Wang CC-B, Hung CT, Ateshian GA: Anisotropic strain-dependent material properties of bovine articular cartilage in the transitional range from tension to compression. *J Biomechanics* 37, 1251-1261, 2004.
32. Kelly TN, Wang CC-B, Mauck RL, Ateshian GA, Hung CT: Role of cell-associated matrix on material development of free-swelling and dynamically loaded chondrocyte-seeded agarose gels. *Biorheology*, 41, 223-237, 2004.
33. Lima EG, Mauck RL, Han S, Park S, Ng KW, Ateshian GA, Hung CT: Functional tissue engineering of chondral and osteochondral constructs. *Biorheology* 41, 577-590, 2004.

34. Takai E, Mauck RL, Hung CT, Guo XE: Osteocyte viability and regulation of osteoblast function in a 3D trabecular bone explant under dynamic hydrostatic pressure. *J Bone Min Res* 19(9):1403-1410, 2004.
35. Ng KW, Wang CC-B, Mauck RL, Kelly TN, Chahine NO, Costa KD, Ateshian GA, Hung CT: A layered agarose approach to fabricate depth-dependent inhomogeneity in chondrocyte-seeded constructs. *J Orthop Res* 23(1), 134-141, 2005.
36. Basalo IM, Mauck RL, Kelly TN, Nicoll SB, Chen FH, Hung CT, Ateshian GA: Cartilage interstitial fluid load support in unconfined compression following enzymatic digestion. *J Biomechanics* 126, 779-786, 2004.
37. Krishnan R, Caligaris M, Mauck RL, Hung CT, Costa KD, Ateshian GA: Removal of the superficial zone of articular cartilage does not increase its frictional coefficient. *Osteoarthritis Cartilage* 12(12), 947-955, 2004.
38. Chao PHG, Tang Z, Angelini E, West AC, Costa KD, Hung CT: Dynamic osmotic loading of cells using a novel microfluidic device. *J Biomechanics* 38(6), 1273-1281, 2005.
39. Basalo IM, Raj D, Krishnan R, Chen FH, Hung CT, Ateshian GA: Effects of enzymatic degradation on the frictional response of articular cartilage in stress relaxation. *J Biomechanics* 38(6), 1343-1349, 2005.
40. Takai E, Costa KD, Shaheen A, Hung CT, Guo XE: Osteoblast elastic modulus measured by atomic force microscopy is substrate dependent. *Ann Biomed Eng*, 33(7), 963-971, 2005.
41. Gupta R, Truong L, Bear D, Chafik D, Modafferi E, Hung CT: Shear stress alters the expression of Myelin Associated Glycoprotein (MAG) and Myelin Basic Protein (MBP) in Schwann cells. *J Orthop Res* 23(5), 1232-9, 2005.
42. Ateshian GA, Likhitpanichkul M, Hung CT: A mixture theory analysis of passive transport in osmotic loading of cells. *J Biomechanics* 39(3):464-75, 2006
43. Kelly TN, Ng KW, Wang CCB, Ateshian GA, Hung CT: Spatial and temporal development of chondrocyte-seeded agarose constructs in free-swelling and dynamically loaded cultures. *J Biomechanics* (June 27 Epub ahead of print), 2005.
44. Chahine NO, FH Chen, Hung CT, Ateshian GA: Direct Measurement of Osmotic Pressure of glycosaminoglycan solutions by membrane osmometry at room temperature. *Biophysical Journal* 89(3), 1543-50, 2005.
45. Ateshian GA and Hung CT: Patellofemoral joint biomechanics and tissue engineering. *Clin Orthop Res Relat Res* 436:81-90.
46. Ishii Y, Thomas AO, Guo XE, Hung CT, Chen FH: Localization and distribution of Cartilage Oligomeric Matrix Protein in the rat intervertebral disc. *Spine* 2005, in press.
47. Takai E, Landesberg R, Katz RW, Hung CT, Guo XE: Substrate modulation of osteoblast adhesion strength, focal adhesion kinase activation, and responsiveness to mechanical stimuli. Submitted to *J Biomed Materials Res*.
48. Ateshian GA, Costa KD, Hung CT: A theoretical analysis of water transport through chondrocytes. *Biomech. Model. Mechanobiol.*, in press.

## BOOK CHAPTERS

1. Mow VC and Hung CT: Chapter 3. Biomechanics of Articular Cartilage in *Basic Biomechanics of the Musculoskeletal System*, 3<sup>rd</sup> edition, ed. N Nordin and V Frankel, Williams & Wilkins, Baltimore, MD, p60-100, 2001.
2. Tang Z, Chao G, Tucay A, Takai E, Djukic D, Lind ML, Hung CT, Guo XE, West A, Osgood R, Yardley JT: XYZ on a Chip: Nanoscale Fabrication, Fluidics, and Optics Directed Toward Applications within Biology and Medicine. In *Organic Nanophotonics* (NATO Science Series. Series II, Mathematics, Physics, and Chemistry, V. 100), eds. F Charra, VM Agranovich, F Kajzar, Kluwer Academic Publishers, p127-138, 2003.

3. Ateshian GA and Hung CT: Chapter 4. Functional Properties for Articular Cartilage and Tissue Engineered Constructs in *Functional Tissue Engineering*, eds. F Guilak, DL Butler, SA Goldstein, DJ Mooney, Springer-Verlag, New York, NY, p46-68, 2003.
4. Mow VC and Hung CT: Chapter 7.2.1.4 Mechanical Properties of Normal and Osteoarthritic Articular Cartilage, and the Mechanobiology of Chondrocytes in *Osteoarthritis*, 3<sup>rd</sup> edition, ed. KD Brandt, S Lohmander and M Doherty, Oxford, Oxford University Press, p102-112, 2003.
5. Guilak F and Hung CT: Physical Regulation of Cartilage Metabolism in *Basic Orthopaedic Biomechanics and Mechanobiology*, 3<sup>rd</sup> edition, eds. VC Mow and R Huiskes, Lippincott Williams & Wilkins, Baltimore, MD, 2005.
6. Hung CT and Mauck RL: Chapter 15: Biological Assays: Cellular Level in *Biomedical Technology and Devices Handbook*, eds. J Moore and G. Zouridakis, CRC Press, Boca Raton, p15.1-15.39, 2003.
7. Kelly TN, Wang CC-B, Mauck RL, Ateshian GA, Hung CT: Role of Cell-associated Matrix on Material Development of Free-Swelling and Dynamically Loaded Chondrocyte-seeded Agarose Gels in *Mechanobiology: Cartilage and Chondrocyte*, ed. J.-F. Stoltz, IOS Press, Amsterdam, The Netherlands, Vol. 3, p223-237, 2004.
8. Lima EG, Mauck RL, Han S, Park S, Ng KW, Ateshian GA, Hung CT: Functional Tissue Engineering of Chondral and Osteochondral Constructs in *Mechanobiology: Cartilage and Chondrocyte*, ed. J.-F. Stoltz, IOS Press, Amsterdam, The Netherlands, Vol. 3. p577-590, 2004.

## CONFERENCE ABSTRACTS

1. Williams JL, Hung CT: A new biaxial testing method for producing uniform and isotropic strains in membranes used as cell or tissue substrates. *Adv Bioeng ASME BED*-26:411-413, 1993.
2. Hung CT, Pollack SR, Reilly TM, Brighton CT: Real-time calcium response of bone cells exposed to fluid flow. Oral presentation and abstract at the 13th Annual Meeting of the Bioelectrical Repair and Growth Society, Dana Point, CA, October 11-14, 1993.
3. Gelb ID, Reilly TM, Brighton CT, Pollack SR, Hung CT: Platelet-derived growth factor stimulation of bone cells: intracellular calcium and inositol trisphosphate as second messengers. *Trans Orthop Res Soc* 19:349, 1994.
4. Reilly TM, Hung CT, Gelb ID, Brighton CT: The effects of calcium second messenger inhibition in the stress-induced proliferation of bone cells. *Trans Orthop Res Soc* 19:274, 1994.
5. Hung CT, Reilly TM, Pollack SR, Brighton CT: Heterogeneous  $[Ca^{2+}]_i$  response in bone cells exposed to fluid flow. *Trans Orthop Res Soc* 19:498, 1994.
6. Hung CT, Reilly TM, Pollack SR, Brighton CT: Real time  $[Ca^{2+}]_i$  measurements in bone cells exposed to fluid flow. BME'94 International Conference on Biomedical Engineering, Hong Kong, April 7-9, 1994.
7. Hung CT, Pollack SR: Heterogeneous  $[Ca^{2+}]_i$  response as a mediator of Wolff's Law in bone cells exposed to laminar fluid flow. *Proceeds of 2nd World Congress of Biomechanics* II:241b, Amsterdam, The Netherlands, July 10-15, 1994.
8. Allen FD, Pollack SR, Gupta R, Hung CT: The intracellular calcium response of osteoblast-like cells to 60 kHz electric field stimulation from 10 V/m to 1 kV/m. *Trans SPRBM* 14:3, 1994.
9. Rau V, Hung CT, Pollack SR: Measuring the zeta potential of primary bone cells. *Trans SPRBM* 14:28, 1994.
10. Hung CT, Allen FD, Pollack SR, Brighton CT: Elucidating the cell signaling pathway in the calcium response of bone cells to fluid flow. *ASME BED* 25:569-570, 1995.
11. Allen FD, Hung CT, Pollack SR, Brighton CT: The effect of newborn bovine serum on the intracellular calcium concentration response of primary cultured bone cells to fluid flow. *Proceeds of 2nd Intl Conference on Cellular Engineering*, p3, La Jolla, CA, August 19-22, 1995.
12. Hung CT, Allen FD, Pollack SR, Brighton CT: The role of the convective current density in the calcium response of cultured bone cells to fluid flow. *Proceeds of the 2nd Inl Conference on Cell Eng*, p46, La Jolla,CA, Aug 19-22, 1995.

13. Allen FD, Hung CT, Pollack SR, Brighton CT: Comparison of the  $[Ca^{2+}]_i$  response of cultured primary, MC3T3-E1, and ROS 17/2.8 osteoblast-like cells to fluid flow. *Trans SPRBM* 15:52, 1995.
14. Hung CT, Allen FD, Mansfield KD, Shapiro IM: Extracellular ATP modulates  $[Ca^{2+}]_i$  in retinoic acid treated embryonic chondrocytes. *Trans Orthop Res Soc* 22(1):7, 1997.
15. Hung CT, Allen FD, Pollack SR, Attia ET, Hannafin JA, Torzilli PA: Comparison of the fluid-induced calcium response of ACL and MCL fibroblasts. *Trans Orthop Res Soc* 22(1):54, 1997.
16. Allen FD, Hung CT, Pollack SR, Brighton CT: Pertussis toxin inhibits cytosolic calcium increases in osteoblast-like cells stimulated by laminar fluid flow incorporating serum. *Trans Orthop Res Soc* 22(1):706, 1997.
17. Allen FD, Hung CT, Pollack SR, Brighton CT: The effect of cell culture passaging on the transduction of fluid flow shear stress in osteoblast-like cells. *Trans Orthop Res Soc* 22(1):707, 1997.
18. Hung CT, Valhmu WB, Ratcliffe A, Mow VC, Allen FD: Articular chondrocyte calcium response to transient fluid-induced shear stress. *Adv Bioeng BED* 35:115-116, 1997.
19. Gu WY, Lai WM, Hung CT, Liu ZP, Mow VC: Analysis of transient swelling and electrical responses of an isolated cell to sudden osmotic loading. *Adv Bioeng BED*-36, 1997.
20. Mow VC, Gu WY, Hung CT, Liu ZP, Lai WM: Transient swelling and electrical responses of cells subject to osmotic shock loading. *Trans 3rd Intl Cell Eng Conference*, San Remo, Italy, 1997.
21. Hung CT, Johnson ED, Allen FD, Litt M, Pollack SR, Meaney DF: Changes in osteoblasts under time averaged microgravity conditions. *Advances in Heat and Mass Transfer in Biotechnology* HTD-355/BED-37, 1997.
22. Hung CT, Valhmu WB, Mow VC, Ratcliffe A: Calcium signaling in articular chondrocytes subjected to transient fluid-induced shear. *Trans Orthop Res* 23(2):897, 1998.
23. Valhmu WB, Hung CT, Mow VC, Ratcliffe A: Fluid flow stimulates the ERK1/2, but not SAPK/JNK, cascade in bovine articular chondrocytes, *Trans Orthop Res* 23(1):184, 1998.
24. Hung CT, Gu WY, Lai WM, Mow VC: Quantification of transient swelling behavior in cultured chondrocytes to osmotic loading, *Trans Orthop Res* 23(2):870, 1998.
25. Hung CT, Attia ET, Bhargava M, Hannafin JA, Torzilli PA: Mechano-chemical coupling in ACL and MCL cells: Calcium response to transient fluid-induced shear stress and bradykinin, *Trans Orthop Res* 23(2): 578, 1998.
26. Hung CT, Wang CB, Henshaw DR, Goldring MB, Valhmu WB: Toward defining the role of  $Ca^{2+}$  and MAP Kinases in fluid-induced shear regulation of aggrecan in chondrocytes. *Advances in Bioengineering BED*-39, p59-60, 1998.
27. Hung CT, Gu WY, Lai WM, Mow VC: A new method to determine mechano-electrochemical properties of cells. *Proceeds of the Third World Congress of Biomechanics*, p215b, Sapporo, Japan, August 2-8, 1998.
28. Hung CT, Gu WY, Lai WM, Mow VC: Chondrocyte swelling experiments and theoretical predictions. *Proceeds of the Third World Congress of Biomechanics*, p111b, Sapporo, Japan, August 2-8, 1998.
29. Palmer G, Ho J, Hung CT, Ratcliffe A, Valhmu WB: MEK-1 regulates aggrecan gene expression through exon 1 (5'UTR). *Trans Orthop Res Soc* 24(1), p81, 1999.
30. Soltz MA, Mauck RL, Hung CT, Ateshian GA: Fluid pressurization in agarose hydrogels under cyclic loading. *Advances in Bioengineering BED*-42, p127-128, 1999.
31. Mow VC, Sun DN, Guo XE, Hung CT, Lai WM: Chondrocyte-extracellular matrix interactions during osmotic swelling. *Adv Bioeng BED*-42, p133-134, 1999.
32. Mauck RL, Jezyk M, Valhmu WB, Hung CT: Chondrocyte shape change and migratory response to DC Electric Fields. *Adv Bioeng BED*-42, p341-342, 1999.
33. Soltz MA, Stankiewicz A, Mauck RL, Hung CT, Ateshian GA: Direct hydraulic permeability measurements of agarose hydrogels used as cell scaffolds. *Advances in Bioengineering BED*-43, 229-230, 1999.
34. Mauck RL, Chao P-H, Gilbert B, Valhmu WB, Hung CT: Chondrocyte translocation and orientation to applied DC electric fields. *Advances in Bioengineering BED*-43, 117-118, 1999.

35. Mauck RL, Soltz MA, Raia FA, Ateshian GA, Valhmu WB, Hung CT: Time-varying effect of ascorbate on the compressive modulus and GAG content of chondrocyte-seeded agarose cultures. *Adv Bioeng* BED-43, 105-106, 1999.

36. Soltz MA, Mauck RL, Hung CT, Ateshian GA: Is articular cartilage orthotropic in compression? *Adv Bioeng* BED-43, 209-210, 1999.

37. Palmer G, Chao PG, Raia F, Mauck R, Valhmu W, Hung CT: Osmotic loading regulates chondrocyte cell size and aggrecan gene expression. *Trans Orthop Res Soc* 25, 924, 2000.

38. Wang, CC-B, Soltz MA, Mauck RL, Valhmu WB, Ateshian GA, Hung CT: Comparison of the equilibrium strain distribution in articular cartilage explants and cell-seeded alginate disks under compression. *Trans Orthop Res Soc* 25, 131, 2000.

39. Soltz MA, Palma C, Barsoumian S, Wang CC-B, Hung CT, Ateshian GA: Multi-axial loading of bovine articular cartilage in unconfined compression. *Trans Orthop Res Soc* 25, 888, 2000.

40. Valhmu W, Palmer G, Wang C, Raia F, Mauck R, Chao P, Hung CT: Fluid flow modulates aggrecan gene expression through the mitogen-activated protein kinase pathway. *Trans Orthop Res Soc* 25, 82, 2000.

41. Mauck RL, Soltz MA, Seruya M, Valhmu WB, Ateshian GA, Hung CT: Characterization of alginate for tissue engineering. *Trans Orthop Res Soc* 25, 200, 2000.

42. Allen FD, Hung CT, Pollack SR, Brighton CT: Fluid flow mechanotransduction to intracellular calcium signalling in primary bone cells depends on fluid-induced shear stress magnitude and loading rate. *Trans Orthop Res Soc* 25, 632, 2000.

43. Allen FD, Hung CT, Pollack SR, Brighton CT: Mechano-chemical coupling in the flow-induced activation of intracellular calcium signaling in primary cultured bone cells. *Trans Orthop Res Soc* 25, 634, 2000.

44. Mauck RL, Palmer GD, Wang CC-B, Soltz MA, Valhmu WB, Ateshian GA, Hung CT. Dynamic compression stimulates the development of equilibrium aggregate modulus in tissue engineered cartilage constructs. *Adv Bioeng* BED-48, p67-68, 2000.

45. Chao P-H, Roy R, Mauck RL, Liu W, Hung CT. Electric field-induced chondrocyte migration: Neomycin effects. *Adv Bioeng* BED-48, p65-66. 2000.

46. Wang CC-B, Guo XE, Deng JJ, Mow VC, Ateshian GA, Hung CT: A novel non-invasive technique for determining distribution of fixed charge density within articular cartilage. *Trans Orthop Res Soc* 26, 129, 2001.

47. Chao P-HG, Palmer G, Valhmu WB, Thomas JL, Hung CT: Characterization of the chondrocyte response to hyperosmotic loading- influence of medium constituents. *Trans Orthop Res Soc* 26, 557, 2001.

48. Hung CT, Jamieson KV, Roy R, Wong DD, Chao P-HG, Sun DDN, Guo XE: Comparison of transient chondrocyte swelling and shrinking behavior. *Trans Orthop Res Soc* 26, 559, 2001.

49. Mauck RL, Seyhan SL, Wang CC-B, Soltz MA, Chao P-HG, Valhmu WB, Ateshian GA, Hung CT: Physiologic loading for cartilage tissue engineering- effect of chondrocyte seeding density. *Trans Orthop Res Soc* 26, 622, 2001.

50. Mauck RL, Wang CC-B, Seyhan SL, Kelly TN, Valhmu WB, Ateshian GA, Hung CT: Seeding density influences the development of mechanical properties in agarose constructs. *Trans Orthop Res Soc* 26, 432, 2001.

51. Soltz, MA, Mauck RL, Hung CT, Lai W, Ateshian GA: Osmotic pressure influence on the frictional response of articular cartilage. *Trans Orthop Res Soc* 26, 60, 2001.

52. Chao P-HG, Palmer GD, Mauck RL, Guo XE, Hung CT: Aggrecan gene expression of chondrocyte seeded 3D hydrogel cultures in response to hypertonic loading. *Adv Bioeng* BED-50, 205-206, 2001.

53. Hung CT and Nicoll SB: Tissue and cell culture techniques: an overview. *Adv Bioeng* BED-50, 317-318, 2001.

54. Hung CT, Costa KD, Guo XE: Apparent and transient mechanical properties of chondrocytes during osmotic loading using triphasic theory and AFM indentation. *Adv Bioeng* BED-50, 625-626, 2001.

55. Takai E, Landesberg R, Katz RW, Hung CT, Guo XE: Osteoblast cell adhesion and focal adhesion kinase activation on various substrates. *Adv Bioeng* BED-50, 669-670, 2001.

56. Mauck RL, Seyhan, SL, Nicoll SB, Ateshian GA, Hung CT: Transforming growth factor  $\beta$ 1 increases the mechanical properties and matrix development of chondrocyte-seeded agarose hydrogels. *Adv Bioeng* BED-50, 691-692, 2001.

57. Wang CC-B, Chahine NO, Kelly TN, Valhmu WB, Hung CT, Ateshian GA: Optical determination of anisotropic material properties of bovine articular cartilage in compression. *Adv Bioeng* BED-50, 719-720, 2001.

58. Hung CT, Chao P-HG, Mauck RL, Guo XE, Mow VC: Chondrocyte aggrecan gene expression in response to hypertonic osmotic loading: comparison of monolayer and 3D studies. Submitted to the Euromech420 Colloquium on Mechanobiology of Cells and Tissues in Nancy, France, April 24-26, 2001.

59. Wang CC-B, Guo XE, Ateshian GA, Mow VC, Hung CT: Determination of the chondrocyte environment within cartilage subjected to loading: theoretical and experimental approach. Submitted to the 2<sup>nd</sup> International Symposium on the Mechanobiology of Chondrocytes and Cartilage in Paris, France, April 27-28, 2001. (satellite meeting of the Euromech420 Colloquium)

60. Mauck RL, Soltz MA, Ateshian GA, Hung CT: Dynamic hydrostatic pressurization increases matrix gene expression by chondrocytes in 3D culture. *Adv Bioeng* IMECE2001/BED-23147.

61. Wang CC-B, Chahine NO, Kelly TN, Lai WM, Hung CT, Ateshian GA: The strain-softening of bovine articular cartilage under infinitesimal deformation in unconfined compression. *Adv Bioeng* IMECE2001/BED-23061.

62. Kelly TN, Wang CC-B, Chahine NO, Ateshian GA, Hung CT: Temporal development of material properties in free swelling chondrocyte-seeded agarose constructs. *Adv Bioeng* IMECE2001/BED-23144.

63. Andarawis NA, Seyhan SL, Mauck RL, Soltz MA, Ateshian GA, Hung CT: A novel device for direct permeation measurements of hydrogels and soft hydrated tissues. *Adv Bioeng* IMECE2001/BED-23149.

64. Lo SS, Mauck RL, Seyhan SL, Palmer GD, Mow VC, Hung CT: Mechanical loading modulates gene expression in chondrocyte-seeded agarose hydrogels. *Adv Bioeng* IMECE2001/BED-23145.

65. Lo SS, LeRoux MA, Chao PG, Palmer GD, Hung CT: The effect of osmolarity on gene expression of chondrocyte monolayer cultures. *Ann Biomed Eng* 29S1, S-28, 2001.

66. Chahine NO, Wang CC-B, Kelly TN, Lai WM, Hung CT, Ateshian GA: The strain-softening of bovine articular cartilage under infinitesimal deformation in unconfined compression. *Ann Biomed Eng* 29S1, S-31, 2001.

67. Ateshian GA, Stark R, Mauck RL, Hung CT: Joint-specific articular surface molds for the production of anatomically shaped tissue-engineered cartilage constructs. *Ann Biomed Eng* 29S1, S-151, 2001.

68. Hung CT, Palmer GD, Chao GP-H, LeRoux MA, Valhmu WB: Differential regulation of hypotonic and hypertonic loading by exon 1 of the human aggrecan gene in chondrocytes. *Trans Orthop Res Soc* 27:137, 2002.

69. Mauck RL, Seyhan SL, Jamieson KV, Nicoll SB, Ateshian GA, Hung CT: Synergistic effects of growth factors and dynamic loading for cartilage tissue engineering. *Trans Orthop Res Soc* 27: 213, 2002.

70. LeRoux MA, Chao GP-H, Palmer GD, Hung CT: Osmotic regulation of chondrocyte gene expression occurs independent of changes in cell morphology and size. *Trans Orthop Res Soc* 27: 384, 2002.

71. Chao GP-H, Nicoll SB, Hung CT: Electric-field induced migration and orientation of ligament fibroblasts and chondrocytes. *Trans Orthop Res Soc* 27: 582, 2002.

72. LeRoux MA, Raina P, Ateshian GA, Guo, XE, Hung CT: Novel composite chondrocyte-seeded agarose-bone constructs for in vitro chondrogenesis. *Trans Orthop Res Soc* 27: 469, 2002.

73. Chahine NO, Wang CCB, Mason JH, Lai WM, Hung CT, Ateshian GA: The roles of osmotic swelling pressure and tension-compression nonlinearity on stress-strain responses of bovine articular cartilage. *Trans Orthop Res Soc* 27: 83, 2002.

74. Wang CCB, Chahine NO, Kelly TN, Hung CT, Ateshian GA: Optical measurements of anisotropic material properties of articular cartilage and determination of its material symmetry in compression. *Trans Orthop Res Soc* 27: 394, 2002.

75. Ateshian GA, Mauck RL, Stark R, Nicoll SB, Hung CT: Joint specific surface molds for articular cartilage tissue engineering. *Trans Orthop Res Soc* 27: 251, 2002.

76. Takai E, Katz RW, Landesberg R, Hung CT, Guo XE: Adhesion strength, focal adhesion kinase activation, and cytoskeletal organization of osteoblasts on various substrates. *Trans Orthop Res Soc* 27: 535, 2002.

77. Guo XE, Shyu J, Takai E, Costa KD, Hung CT: Substrates influence osteoblast elastic modulus measured by atomic force microscopy. *Trans Orthop Res Soc* 27: 521, 2002.

78. Tang Z, Chao G, Tucay A, Takai E, Djukic D, Lind ML, Hung CT, Guo XE, West A, Osgood R, Yardley JT: XYZ on a chip: nanoscale fabrication, fluidics, and optics directed toward applications within biology and medicine. NATO Organic Nanophotonics, Aix-en-Provence, France, August 2002.

79. Chao PG-C, Angelini E, Tang Z, Chang W., Bulinski JC, West AC, Hung CT: Novel application of microfluidic channels in studying cell migration and reorientation in response to direct current electric fields. IMECE2002-33138, 2002.

80. Nicoll SB, Mauck RL, Tsay RC, Hung CT, Ateshian GA: Intermittent hydrostatic pressurization modulates gene expression in human dermal fibroblasts seeded in 3D polymer scaffolds. IMECE2002-33604, 2002.

81. Takai E, Hung CT, Tucay A, Djukic D, Linde ML, Costa KD, Yardley J, Guo XE: Design of a microfluidic system for 3D culture of osteocytes in vitro. IMECE2002-33229, 2002.

82. Takai E, Guo XE, Lu HH, LeRoux MA, Raina P, Ateshian GA, Hung CT: Strategy for tissue engineering of osteochondral constructs. IMECE2002-33595, 2002.

83. Chahine NO, Wang CC-B, Hung CT, Ateshian GA., 2002, Determination of Poisson's Ratios of Bovine Articular Cartilage in Tension and Compression Using Osmotic and Mechanical Loading. IMECE2002-32622

84. Ateshian GA, Mauck RL, Hung CT: Modeling of neutral solute transport in a dynamically loaded porous permeable gel: implications for articular cartilage biosynthesis and tissue engineering. To be presented at the Symposium on the Mechanics of Physiochemical and Electromechanical Interactions in Porous Media, May 18-23, 2003, Rolduc, kerkrade, The Netherlands.

85. Lu HH, Jiang J, Hung CT, Lima E: Characterization of a composite scaffold with intended application in osteochondral grafting. Musculoskeletal Biology & Bioengineering Gordon Conference, Proctor Academy, Andover, New Hampshire (poster presentation), July 28-August 2, 2003

86. Ateshian GA, Mauck RL, Wang CCB, Park S, Lima E, Lu HH, Chen H, Guo XE, Hung CT: The role of dynamic loading in cartilage functional tissue engineering. Presented at the Tissue Engineering Conference, Cold Spring Harbor Laboratory, Long Island, NY, November 21-24, 2002.

87. Takai E, Lima E, Lu HH, Ateshian GA, Guo XE, Hung CT: Devitalized bone as a mineralized substrate for osteochondral tissue engineered hydrogel constructs. *Trans Orthop Res Soc* 28: 307, 2003.

88. Chahine NO, Wang CCB, Kelly TN, Elbeshbeshy R, Mauck RL, Hung CT, Ateshian GA: The effect of finite compressive strain on chondrocyte viability in statically loaded bovine articular cartilage. *Trans Orthop Res Soc* 28: 646, 2003.

89. Kim CH, Han SH, Chen FH, Ateshian GA, Hung CT, Guo XE: Intervertebral disc response to in vivo dynamic loading in a rat-tail model. *Trans Orthop Res Soc* 28: 57, 2003.

90. Mauck RL, Hung CT, Ateshian GA: Modeling solute transport with mixture theory for dynamically loaded porous permeable gels. *Trans Orthop Res Soc* 28: 662, 2003.

91. Ng, K, Wang CCB, Guo XE, Ateshian GA, Hung CT: Characterization of inhomogeneous bi-layered chondrocyte-seeded agarose constructs of differing agarose concentrations. *Trans Orthop Res Soc* 28: 960, 2003.

92. Mauck RL, Lima EG, Oswald ES, Hung CT, Ateshian GA: Hydrostatic pressure increases matrix deposition and material properties of chondrocyte-seeded agarose hydrogels. 2003 *Trans Orthop Res Soc* 28: 685, 2003.

93. Nicoll SB, Mauck RL, Bordone LA, Tsay R, Hung CT, Ateshian GA: Hydrostatic pressure stimulates expression of fibrocartilaginous extracellular matrix proteins in human dermal fibroblasts seeded in 3-D polymer scaffolds. *Trans Orthop Res Soc* 28: 950, 2003.

94. Hung CT, Lima EG, Mauck RL, Lu HH, Ateshian GA: Considerations for the design of biphasic anatomically-shaped constructs for articular cartilage tissue-engineering. *Trans Orthop Res Soc* 28: 971, 2003.

95. Kelly TN, Wang CCB, Mauck RL, Chahine NO, Ateshian GA, Hung CT: Effects of dynamic loading on material properties of chondron-seeded hydrogels. *Trans Orthop Res Soc* 28: 132, 2003.

96. Mauck RL, Wang CCB, Cheng Q, Gabriel N, Oswald ES, Ateshian GA, Hung CT: Optimization of parameters for articular cartilage tissue engineering with deformational loading. *Trans Orthop Res Soc* 28: 305, 2003.

97. Chao PG, Han SH, Nicoll SB, Hung CT: ACL and MCL fibroblast migration in response to an applied DC electric field. *Trans Orthop Res Soc* 28: 673, 2003.

98. Chao PG, Tang X, Angelini E, West AC, Hung CT: A novel microfluidic device to study the real-time response of cultured cells to applied dynamic osmotic loading. *Trans Orthop Res Soc* 28: 252, 2003.

99. Bear D, Warren C, Bui P, Chafik D, Hung CT, Gupta R: Schwann cells remain promyelinogenic after being subjected to sustained shear stress. *Trans Orthop Res Soc* 28: 96, 2003.

100. Takai E, Kinnebrew GH, Hung CT, Guo XE: Co-culture of osteocytes and osteoblasts in a 3D trabecular bone explant. *Trans Orthop Res Soc* 28: 308, 2003.

101. Ho MMY, Ng KW, Mauck RL, Ateshian GA, Hung CT: Gelling temperature and gel concentration effects on tissue development in chondrocyte-seeded agarose hydrogels. *Adv Bioeng* (0355.pdf), 2003.

102. Lima EG, Mauck RL, Park S, Gasinu S, Ng KW, Hung CT, Ateshian GA: Material properties of osteochondral constructs and biphasic finite element models of dynamic loading for articular cartilage tissue engineering. *Adv Bioeng*(1129.pdf), 2003.

103. Mauck RL, Ho MMY, Hung CT, Ateshian GA: Growth factor supplementation and dynamic hydrostatic pressurization for articular cartilage tissue engineering. *Adv Bioeng* (0283.pdf), 2003.

104. Mauck RL, Wang CCB, Chen FH, Lu HH, Ateshian GA, Hung CT: Dynamic deformational loading of chondrocyte-seeded agarose hydrogels modulates deposition and structural organization of matrix constituents. *Adv Bioeng* (0531.pdf), 2003.

105. Mauck RL, Oswald ES, Cheng Q, Majumdar MK, Nicoll SB, Ateshian GA, Hung CT: Hydrostatic pressure enhances chondrogenic differentiation of human mesenchymal stem cells in alginate disks. *Adv Bioeng* (0265.pdf), 2003.

106. Wang CCB, Kelly TN, Mauck RL, Ateshian GA, Hung CT: Temporal and spatial development of construct stiffness in chondrocyte-seeded agarose disks cultured in free-swelling and dynamically loaded configurations. *Adv Bioeng* (0279.pdf), 2003.

107. Kelly TN, Wang CCB, Mauck RL, Ateshian GA, Hung CT: Effects of seeding density and native pericellular matrix on the response of chondrocytes to dynamic loading. *Adv Bioeng* (0187.pdf), 2003.

108. Chao PHG, Tang Z, West AC, Hung CT: Chondrocyte size changes in response to cyclic hypertonic loading using a novel microfluidic device. *Adv Bioeng* (1127.pdf), 2003.

109. Costa KD, Ho MMY, Hung CT: Multi-scale measurement of mechanical properties of soft samples with atomic force microscopy. *Adv Bioeng* (0285.pdf), 2003.

110. Takai E, Mauck RL, Hung CT, Guo XE: Osteocyte interaction with osteoblasts and response to intermittent hydrostatic pressure loading in a 3D trabecular bone explant culture model. *Adv Bioeng* (0183.pdf), 2003.

111. Chahine NO, Wang CCB, Elbeshbeshy RR, Hung CT, Ateshian GA: Depth-dependent orthotropic tensile and compressive properties of human patellar cartilage. *Adv Bioeng* (0563.pdf), 2003.

112. Chahine NO, Mantzaris AA, Chen FC, Hung CT, Ateshian GA: Direct measurement of osmotic pressure of glycosaminoglycan solutions. *Adv Bioeng* (1145.pdf), 2003.

113. Park S, Krishnan R, Hung CT, Ateshian GA: In situ measurement of the dynamic modulus of bovine humeral head articular cartilage under physiological contact loading conditions. *Adv Bioeng* (1207.pdf), 2003.

114. Canal C, Meade NK, Park S, Wang CCB, Hung CT, Ateshian GA: Optical measurement of in situ strain fields within osteochondral tissue under indentation. *Adv Bioeng* (0363.pdf), 2003.

115. Moa-Anderson BJ, Costa KD, Hung CT, Ateshian GA: Bovine articular cartilage surface topography and roughness in fresh versus frozen tissue samples using atomic force microscopy. *Adv Bioeng* (0561.pdf), 2003.

116. Mauck RL, Ateshian GA, Hung CT: Theoretical considerations for functional cartilage tissue engineering. 3<sup>rd</sup> International Symposium on Mechanobiology of Cartilage and Chondrocytes, May 17, 2003, Brussels, Belgium.

117. Kelly TN, Oswald ES, Mauck RL, Ateshian GA, Hung CT: Reducing serum dependence: tissue engineering of cartilage in ITS supplemented media. *Trans Orthop Res* 29:725, 2004.

118. Kelly TN, Ho MMY, Mauck RL, Ateshian GA, Hung CT: Effects of pre-elaborated ECM on development of functional properties in chondrocyte-seeded agarose constructs subjected to physiologic deformational loading. *Trans Orthop Res* 29:695, 2004.

119. Lima EG, Mauck RL, Gasinu S, Ateshian GA, Hung CT: Functional tissue engineering of free-swelling and dynamically loaded osteochondral constructs. *Trans Orthop Res* 29:13, 2004.

120. Chahine NO, DuBois CR, Ateshian GA, Hung CT: Optical determination of strain fields at the interface between graft and articular cartilage in an in vitro model of cartilage repair. *Trans Orthop Res* 29:174, 2004.

121. Mauck RL, Chahine NO, Lima EG, Hung CT, Ateshian GA: Functional tissue formation: from bulk properties to cellular microenvironments. *Trans Orthop Res* 29:309, 2004.

122. Chao PHG, Cannon AM, Costa KD, Hung CT: Effects of basal osmolarity on chondrocyte transient behavior to step osmotic loading. *Trans Orthop Res* 29:538, 2004.

123. Ng KW, Mauck RL, Ateshian GA, Hung CT: Dynamic loading modulates the inhomogeneity of bi-layered chondrocyte-seeded agarose constructs of differing agarose concentrations. *Trans Orthop Res* 29:842, 2004.

124. Han S, Ho MMY, Kim CH, Chen FH, Weidenbaum M, Ateshian GA, Hung CT, Guo XE: In vivo hyperphysiologic load at high frequencies is detrimental to intervertebral disc composition in rat tails. *Trans Orthop Res* 29:22, 2004.

125. Jiang J, Hung CT, Guo XE, Ateshian GA, Lu HH: Three dimensional degradable, bioactive polymer ceramic-hydrogel composite for osteochondral repair. *Trans Orthop Res* 29:15, 2004.

126. Krishnan R, Caligaris M, Mauck RL, Hung CT, Costa KD, Ateshian GA: Removal of the superficial zone of bovine articular cartilage does not increase its frictional coefficient. *Trans Orthop Res* 29:172, 2004.

127. Cai W, Thomas AO, Hung CT, Chen FH: Role of COMP in chondrocyte ERK signaling pathway activation. *Trans Orthop Res* 29:594, 2004.

128. Takai E, Hung CT, Costa KD, Yardley JT, Guo XE: Controlled culture of bone cellular networks in 2D and 3D. *Trans Orthop Res* 29:376, 2004.

129. Takai E, Huang MS, Mauck RL, Hung CT, Guo XE: Osteocytes regulate osteoblast function in a 3D trabecular bone explant under dynamic hydrostatic pressure. *Trans Orthop Res* 29:90, 2004.

130. Chahine NO, Chen FH, Hung CT, Ateshian GA: Direct measurement of the osmotic pressure of glycosaminoglycan solutions at room temperature in sodium chloride. *Trans Orthop Res* 29:524, 2004.

131. Hung CT, Kelly TN, Lima EG, Ng KW, Ateshian GA: A Functional Tissue Engineering Strategy for Repair and Replacement of Osteoarthritic Cartilage, Presented at the European Society of Biomechanics 2004, the Netherlands, July 4-7, 2004.

132. Likhitpanichkul M, Chao PG, Hung CT, Ateshian GA: Determination of modulus and permeability of chondrocytes from cell response to osmotic loading. Presented at the European Society of Biomechanics 2004, the Netherlands, July 4-7, 2004.

133. Chao PG, Navratil FR, Hung CT: Effects of basal osmolarity on chondrocyte cell size change and intracellular calcium response to step osmotic loading. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

134. Ng KW, Kelly TN, Chahine NO, Costa KD, Ateshian GA, Hung CT: Development of functional properties of bi-layered chondrocyte-seeded agarose constructs. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

135. Hung CT, Lima EG, Ng KW, Kelly TN, Chahine NO, Mauck RL, Costa KD, Ateshian GA: Applied deformational loading to promote/guide development of chondrocyte-seeded agarose constructs. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

136. Takai E, Mauck RL, Huang MS, Hung CT, Guo XE: Osteocyte and osteoblast response to dynamic hydrostatic pressure in a 3D trabecular explant. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

137. Morrison B, Cater HL, Wang C, Davis S, Lennon J, Ateshian GA, Hung CT: A detailed mechanical tolerance criterion for living brain at the tissue level. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

138. Fan C, Ho W, Chao PG, Hung CT, Morrison B: Osmotic loading of astrocytes: implications for post-traumatic edema. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

139. Basalo IM, Ateshian GA, Hung CT: Effect of chondroitinase ABC on the equilibrium frictional properties of articular cartilage. Presented at the 2004 BMES Annual Meeting, Philadelphia, PA, October 13-16.

140. Moffat K.L., Chahine N.O., Hung C.T., Ateshian G.A., Lu H.H., 2005, Mechanical Properties of Fibrocartilage At the ACL Insertion Site. *International Symposium on Ligaments and Tendons-V*. Washington D.C.

141. Gupta R. et al: Shear stress alters the expression of myelin associated glycoprotein and myelin basic protein in schwann cells. *Trans Orthop Res Soc* 30: 225, 2005

142. Ho MM, Ng KW, Capiola D, Weidenbaum M, Ateshian GA, Guo XE, Hung CT: A rat-tail in vivo bioreactor for physiologic loading of engineered tissue constructs. *Trans Orthop Res Soc* 30: 261, 2005

143. Ho MM, Ateshian GA, Hung CT: Determination of in situ strain fields in rat tail intervertebral disc under axial compressive loading. *Trans Orthop Res Soc* 30: 271, 2005.

144. Ng KW, Saliman JD, Kelly TN, Statman LY, Ateshian GA, Hung CT: Collagen hydrolysate increases the mechanical properties and type II collagen synthesis of tissue engineered articular cartilage. *Trans Orthop Res Soc* 30: 259, 2005.

145. Chao PG, Han S, Costa KD, Hung CT: Chondrocyte calcium signaling is modulated by dynamic osmotic loading. *Trans Orthop Res Soc* 30: 906, 2005.

146. Cook JL, Lima EG, Hung CT, Ateshian GA, Kuroki K, Stoker AM, Fox DB: In vitro and in vivo evaluation of tissue-engineered constructs for articular cartilage regeneration. *Trans Orthop Res Soc* 30: 1767, 2005.

147. Ho MM, Ng KW, Kelly TN, Ateshian GA, Kuroki K, Cook JL, Hung CT: Synoviocyte potential for articular cartilage tissue engineering and repair. *Trans Orthop Res Soc* 30: 1789, 2005.

148. Ng KW, Saliman JD, Kelly TN, Statman LY, Ateshian GA, Hung CT: Hyaluronan modulates the material properties and biochemical content of dynamically-loaded chondrocyte-seeded agarose constructs. *Trans Orthop Res Soc* 30: 1787, 2005.

149. Kelly TN, Ng KW, Lee EJ, Lima EG, Statman LY, Doty SB, Costa KD, Ateshian GA, Hung CT: Development of radial properties of engineered articular cartilage using unconfined compression. *Trans Orthop Res Soc* 30: 1788, 2005.

150. Han SH, Chao PG, Palmer GD, Hung CT: Influence of serum on hypotonic loading-induced chondrocyte mechanotransduction. *Trans Orthop Res Soc* 30: 1633, 2005.

151. Chahine NO, Lima EG, Victor W, Hung CT, Ateshian GA: Dynamic deformational loading significantly enhances the transport of dextran molecules into agarose hydrogels. *Trans Orthop Res Soc* 30: 1791, 2005.

152. Kelly TN, Fisher MB, Lima EG, Ateshian GA, Hung CT: Integrative properties of chondrocyte-seeded agarose constructs. *Trans Orthop Res Soc* 30: 1790, 2005.

153. Takai E, Hung CT, Costa KD, Guo XE: Substrate modulation of osteoblast modulus and response. *Trans Orthop Res Soc* 30: 333, 2005

154. Takai E, Xu Q, Jiang, XJ; Whitesides GM, Costa KD, Yardley JT, Hung CT, Guo XE: Calcium signaling in controlled 2-dimensional bone cell cultures. *Trans Orthop Res Soc* 30:56, 2005

155. Chahine N.O., Lima E.G., Ateshian G.A., Hung CT, 2005, Effect of Dynamic Loading on the Transport of Solutes into Agarose Hydrogels, 4<sup>th</sup> Annual International Symposium on Mechanobiology of Cartilage and Chondrocyte, Budapest, Hungary.

156. Albro MB, Chahine NO, Ng KW, Likhitpanichkul M, Hung CT, Ateshian GA: Osmotic loading of alginate gels: a biomimetic study of hindered transport in the cell cytoplasm. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

157. Ho MM, Kelly TN, Ateshian GA, Hung CT: Rat tail intervertebral disc mechanical response with intact and excised nucleus pulposus. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

158. Ng KW, Statman LY, Ateshian GA, Hung CT: Evaluation Of Hyclone Bovine Growth Serum For Use In Cartilage Tissue Engineering. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

159. Chao PG, Hung CT: Effects of dynamic osmotic loading on chondrocyte calcium response and gene expression. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

160. Chao PG, Hung CT: Effects of constant and pulsed direct current electric fields on ACL fibroblast migration and gene expression. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

161. Lima EG, Setti P, Ateshian GA, Cook JL, Cook CR, Hile DD, Hung CT: Tissue engineering of cylindrical and anatomically-shaped osteochondral constructs using poly (propylene glycol-co-fumaric acid) as a moldable, porous substrate. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

162. Chahine NO, Chen FH, Hung CT, Ateshian GA: The contribution of osmotic pressure to the effective compressive aggregate modulus of bovine articular cartilage. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

163. Chahine NO, Lima EG, Wei VI, Hung CT, Ateshian GA: Effect of simultaneous application of direct perfusion and dynamic loading on the transport of dextran into agarose hydrogels. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

164. Kelly TN, Chahine NO, Fisher MB, Ng KW, Tai T, Ateshian GA, Hung CT: Tension-compression nonlinearity in chondrocyte-seeded agarose hydrogels. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

165. Oswald ES, Chao PG, Hung CT: The effects of osmotic loading on bovine chondrocyte and BMSC cell shape change and intracellular calcium response. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO.

166. Moffat KL, Chahine NO, Hung CT, Ateshian GA, Lu HH: Characterization of the mechanical properties of the ACL-bone insertion site. *Proceedings of the 2005 Summer Bioengineering Conference*, Vail, CO. (First Place in Master's Poster Competition in Cell/Tissue Engineering Category)

167. Hung CT, Kelly TN, Chahine N.O., Ateshian GA, 2005, Cartilage Tissue Engineering: Implications of Applied Deformational Loading and Solute Transport, *Annals of Biomedical Engineering*, Baltimore, MD, Abstract #142478.

## ACTIVE GRANTS

- Principal Investigator:** NIH: NIAMS 2R01AR46568-05A2: *Physiologic loading for cartilage tissue engineering*; approximate yearly direct cost:\$200,000, 4/1/05-12/31/08 (total cost for entire granting period: \$1,200,000)- 25% yearly effort. Description: This COMPETING RENEWAL continues our investigation of the use of applied physiologic loading in a custom bioreactor to grow functional articular cartilage. Bovine/canine chondrocytes are encapsulated in agarose hydrogels and subjected to physiologic loading in long-term cultures. Tissue material properties and biochemical composition are measured and compared to those of native cartilage. The aims of the grant are extended to study the effects of combined deformational loading with direct media perfusion, as well as the effects of loading boundary conditions on the development of tissue inhomogeneity and surface properties.

2. **Principal Investigator:** NIH: NIAMS 1R01 AR49922-04: *Intervertebral disc response to cyclic loading in vivo*, \$164,500 yearly direct cost (\$1,041,497 total cost), 9/26/02-8/31/06, 20% yearly effort. Description: The aim of this grant is to investigate the material and biochemical properties (e.g., aggrecan, collagen and cartilage oligomeric matrix protein) of the intervertebral disc subjected to well-controlled loading regimens in an *in vivo* rat-tail model.
3. **Co-Investigator:** NIH: NIAMS 1R01AR46532-05 (Ateshian PI): *Anisotropy and nonlinearity of cartilage mechanics*; approximate yearly direct cost: \$200,000, 2/1/04-1/31/09 (total cost for entire granting period: \$1,571,996)- 20% yearly effort. Description: This COMPETING RENEWAL continues to develop a model for articular cartilage that can explain its anisotropic and nonlinear behavior (in tension and compression). It proposes a hierachial series of progressively more complex experiments from the joint to the cellular level. Dr. Hung plays a role primarily in the measurement of cartilage material properties and tissue inhomogeneity, and local strain environment around the cell using custom loading devices mounted on an epifluorescence microscopy system.
4. **Co-Investigator:** NIH: NIAMS R01 AR43628-09 (Ateshian, PI): *Biotribology of diarthrodial joints*; (total cost: \$1,766,739)- 6/1/04-5/31/09- 10% yearly effort. This grant represents a competing renewal that will use AFM, TIRF and custom testing devices to assess the role of the superficial zone and potential lubricants (such as lubricin or SZP protein) on diarthrodial joint lubrication.
5. **Co-Principal Investigator:** National Science Foundation (NSF) MCB-0423475 (J. Chloe Bulinski, PI): *Probing mechanisms of cell motility in electric fields* (total cost: \$350,001)- 8/1/04-7/31/06- one month summer support. Description: This grant will investigate mechanisms (e.g., cell surface charge, enzymatic treatments, polycation and polyanions, cytoskeleton) on 3T3 Fibroblast orientation and directed migration to DC electric fields, in sparse and wounded monolayer cultures. Bioengineering analysis and microfluidic systems will be applied.
6. **Co-Investigator:** NIH R21 AR052417-01A1 (Edward Guo, PI): *Microfluidics and Bone Mechanotransduction*; granting period: \$275,000 total direct costs- 10% effort, 1/01/06-12/31/07. Description: Use microfluidic technology to study osteocyte and osteoblast mechanotransduction to mechanical stimuli in a 2D and 3D model system. The role of cell-cell communication will be examined with respect to gap junction role in mediating intracellular calcium transients measured using fluorescence microscopy.
7. **Consortium Principal Investigator:** NIH 1R21AR053530-01 subcontract from University of Missouri (James L. Cook, PI): *Tissue engineered osteochondral patella resurfacing*; total costs: \$420,323 (total subcontract amount \$165,000)- 2.5% effort, 3/1/06-2/28/08. Description: This application seeks to fabricate a tissue engineered osteochondral patella construct for implantation in a canine *in vivo* model. The Columbia subcontract will take canine cells from the Comparative Orthopaedic Laboratory and culture osteochondral patella constructs that will subsequently be implanted into canine knees in Missouri.

## GRANTS PENDING

1. **Principal Investigator:** NIH: NIAMS 1R01AR052871-01A1: *Chondrocyte mechanotransduction using microfluidics*, 25% yearly effort; approximate yearly direct costs: \$225,000, 4/1/06-3/31/10 (total cost for entire granting period: \$1,400,000). Description: This grant will study the dynamic osmotic loading response of cultured chondrocytes using a custom microfluidics device. The role of cell size change and osmotic load magnitude/frequency on the intracellular calcium signaling response and subsequent cytoskeletal rearrangement and aggrecan gene expression of chondrocytes will be assessed. (SCORE: 161; 9.1%)
2. **Co-Investigator:** NIH (Gerard Ateshian, PI): *Solute transport in cartilage tissue engineering*; 20% academic and 33% summer effort, 12/01/05-11/30/09. Description: This grant will investigate the use of mixture theory to model deformational loading-induced solute transport in hydrogel constructs as a potential mediator of enhanced tissue construct growth observed with daily applied deformational loading. Theoretical analyses will be complemented with experimental methodologies including photobleaching studies for determination of solute diffusion coefficients, direct hydraulic permeability and Aggregate modulus measurements of constructs, and confocal microscopy of solute transport real-time in axially loaded cell-free and cell-seeded cylindrical constructs.

## PAST GRANTS

1. **Principal Investigator:** (subcontract from University of Wisconsin) NIH: NIAMS R01 AR45753 (Wilmot Valhmu PI): *Flow-induced MAPK and calcium signaling in chondrocytes*; approximate yearly direct cost: \$87,262, 4/1/00-8/30/02 (co-PI of original grant received 9/98), (total cost for entire granting period: \$115,090)- 25% academic and 33% summer effort. Description: The aim of this grant is to elucidate the role of mitogen activated protein kinases and calcium in chondrocyte mechanotransduction to fluid-induced shear stress. A major component of the grant is to delineate between concomitant stimuli that exist in the flow studies (e.g., electrokinetic phenomena, transport, shear rate).
2. **Principal Investigator:** Whitaker Biomedical Research Grant: *Shape changes and directed migration in chondrocytes to DC electric fields*; approximate yearly direct cost: \$70,000, 5/1/99-4/30/02 (total cost for entire period: \$209,999)- 20% annual effort. Description: This grant examines the mechanism behind chondrocyte galvanotropism and galvanotaxis, shape change and directed migration in response to applied direct current electric fields. Studies include the examination of cell surface charge, cell-substrate interactions, and nature of the applied electric field stimulus.
3. **Principal Investigator:** (subcontract from Conversion Energy Enterprises, Spring Valley, NY; SBIR Phase I) NIH: NIAMS 1R43AR48738-01 (Soltz PI): *Laser-assisted cartilage repair using collagen adhesives*; \$30,000 total cost, 5/15/02-10/15/02- 10% effort. Description: The aim of this grant is to investigate the efficacy of laser activated collagen formulations as an adhesive and as an acellular graft that permits and/or promotes cell invasion.
4. **Principal Investigator:** Whitaker Foundation: *Transitional Funding: Microfluidic device for osmotic loading of cultured chondrocytes* (\$80,000 total cost), 5/1/02-4/30/03, 20% yearly effort. Description: The aim of this grant is to develop a microfluidic device capable of subjecting cultured chondrocytes to time-varying osmotic loading while permitting study of their biological response (e.g., cell shape and volume change, aggrecan gene expression).
5. **Principal Investigator:** NIH: NIAMS 1R01AR46568-04 *Supplement*: approximate yearly direct cost: \$29,000, 1/1/00-12/31/03 (total cost for entire granting period: \$157,519) Description: Minority supplement for Terri-Ann Kelly (GRA) to expand the aims of the parent grant to study the development of inhomogeneous material and biochemical composition of chondrocyte-seeded agarose disks subjected to physiologic loading, using a microscopy-based system to measure tissue strains using a digital image correlation technique.
6. **Co-Investigator:** NIH: NIAMS 1R01AR46532-04 (Gerard Ateshian PI): *Anisotropy and nonlinearity of cartilage mechanics*; approximate yearly direct cost: \$124,711, 2/1/00-1/31/03 (total cost for entire granting period: \$724,337)- 20% academic and 30% summer effort. Description: This aim of this grant is to develop a model for articular cartilage that can explain its anisotropic and nonlinear behavior (in tension and compression). Dr. Hung plays a role primarily in the measurement of cartilage material properties and tissue inhomogeneity using custom loading devices mounted on an epifluorescence microscopy system.
7. **Co-Investigator/Consultant:** The Aircast Foundation (Ranjan Gupta PI): *Schwann cell response to the biomechanical forces associated with carpal tunnel syndrome*, \$50,000/year, 6/03-5/05- 5% effort year 1. Description: This grant, awarded to Dr. Ranjan Gupta at UC Irvine, investigates the Schwann cell response to a reproducible, quantifiable mechanical stimuli in a controlled, physiologic environment. These studies will utilize parallel plate flow chambers and use various strategies to delineate between concomitant flow related stimulus in regulation of pro-myelogenic markers (MBP, MAG) as well as iNOS and VEGF mRNA.
8. **Principal Investigator:** NIH administrative supplement for nano-scale research related to NIAMS 1R21 AR48791-03. *Supplement for incorporation of laser tweezers* (\$50,000 total cost), 9/30/03-9/29/04. Supplement to establish research collaboration with Dr. Michael Sheetz, Department of Biological Sciences at Columbia University, to incorporate laser tweezers and magnetic bead pulling system to the project.
9. **Principal Investigator:** National Institutes of Health (NIH): National Institutes of Arthritis, Musculoskeletal and Skin Diseases (NIAMS) 1R01AR46568-05: *Physiologic loading for cartilage tissue engineering*; approximate yearly direct cost: \$143,890, 1/1/00-12/31/04 (total cost for entire granting period: \$831,444)- 20% academic and 33% summer effort. Description: This grant investigates the

use of applied physiologic loading in a custom bioreactor to grow functional articular cartilage. Bovine chondrocytes are encapsulated in agarose hydrogels and subjected to physiologic loading in long-term cultures. Tissue material properties and biochemical composition are measured and compared to those of native cartilage. (no cost extension)

10. **Principal Investigator:** NIH: NIAMS 1R21 AR48791-03: *Novel Determination of chondrocyte material properties*; \$75,000 yearly direct cost (\$350,762 total cost), 7/1/02-6/30/05- 10% yearly effort. Description: The aim of this grant is to develop novel techniques to determine cell material properties using osmotic loading, videomicroscopy, Atomic Force Microscopy, and theoretical and computational modeling.
11. **Principal Investigator:** NIH: NIAMS 1R01AR49922-03 *Supplement*: approximate yearly direct cost:\$43,000, 1/1/04-6/30/05 (total cost for entire granting period: \$86,285) Description: Minority supplement for Terri-Ann Kelly (GRA) to expand the aims of the parent grant to study the inhomogeneous material and biochemical composition of rat IVD subjected to well-controlled loading regimens in an in vivo rat-tail model.

## OTHER

**Date of Birth:** May 18, 1968  
**Place of Birth:** Springfield, Massachusetts, USA  
**Marital Status:** Spouse: Luci Morrone, M.D., M.P.H. (Pediatrician)  
**Hobbies:** Tennis, Alpine Skiing, Piano/Keyboards ([www.roostrock.com](http://www.roostrock.com))